

## Evaluation of first trimester fasting blood glucose as a predictor of gestational diabetes mellitus

Reshma Shri Aravind<sup>1,\*</sup>, Latha Maheshwari<sup>2</sup>, Aravind Chander<sup>3</sup>

<sup>1,3</sup>Consultant, Iswarya Women's Hospital & Fertility Center, Tamil Nadu, <sup>2</sup>Professor, Dept. of Obstetrics & Gynecology, PSG Hospital, Tamil Nadu

**\*Corresponding Author:**

Email: reshmashri9@gmail.com

### Abstract

**Background:** Our goal was to find association between first trimester fasting blood sugar value compared with the second trimester oral glucose tolerance test value (75gm DIPSI criteria) for diagnosis of GDM. To find the efficiency of FBS and BMI as a screening test for GDM.

**Material and Method:** 270 antenatal patients having antenatal follow up from 1<sup>st</sup> trimester of pregnancy between June 2014 – May 2015. The study period was 12 months. Their fasting blood glucose levels was measured in first trimester. The patients were followed up during second trimester and 75 grams OGTT was done. Correlation between first trimester FBS, BMI versus second trimester OGTT were done. Screening property of both fasting blood sugar and BMI were calculated and compared using receiver operating characteristic (ROC) curves.

**Result:** Out of 270 patients, 14 patients developed GDM, 1 patient developed overt diabetes. With threshold of FBS>90 yielded sensitivity of 86%, specificity of 52%. FBS >90mg/dl can be considered as a threshold value for predicting GDM. With a threshold of BMI>24 yielded sensitivity of 60%, specificity of 67.5%, hence BMI >24 is a good predictor of GDM. Receiver operating characteristic curve shows FBS(AUC-0.69) has little more discriminatory power in identifying GDM than BMI(AUC=0.63). P value <0.05 was considered statistically significant.

**Conclusion:** In conclusion, FBS measurement at first prenatal visit or at first booking will be useful to screen for previously undiagnosed pre-existing diabetes mellites and also help to predict the development of GDM earlier.

**Keywords:** Gestational, Diabetes mellites, Fasting, Blood, Sugar, BMI

### Introduction

GDM is defined as —glucose intolerance of variable degree with onset or first recognised during pregnancy. GDM has been recently reported to affect approximately 18% of pregnancies. According to World Health Organisation India has the largest number of cases of Diabetes in the world. As estimated 31.7 million people with diabetes in 2000 in India are projected to increase to 79.4 million in 2030.<sup>(1)</sup> Women who are diagnosed with gestational diabetes have an increased chance (35% to 60%) of developing diabetes in the next 1-2 decades and the predicted health care expenses are definitely going to be high.

Many of these women were amenorrhoeic and only about 2% of diabetic patients conceived. The diabetic patients who conceived had an increased risk of morbidity and mortality.

Poor sugar control in mother lead to poor maternal and perinatal outcomes. There is approximately 42.9% chances of perinatal mortality. With proper diagnosis and treatment of GDM, the perinatal and maternal outcome can be increased.

Intrauterine exposure of increased sugar levels has a negative impact on the pregnancy and also lead to glucose intolerance in the offspring latter period of life.

No uniform guidelines for the management of GDM exist on a local, national or global level. Given the high rate of hyperglycaemia in pregnancy, selective testing based on known risk factors has poor sensitivity for

detecting GDM, universal rather than risk factor-based testing seem to be more practical. Universal testing is recommended by several organizations including International Association of Diabetes and Pregnancy study Group (IADPSG), Diabetes In Pregnancy Study group India (DIPSI). Asian Indian women are considered to be at the highest risk of GDM and therefore require universal testing.

In India, approximately 27 million births occur annually requiring at least 27 million OGTTs annually; considering a 10% average prevalence of GDM, the number of GDM pregnancies would be around 2.7 million, a huge burden to deal with for any health system. Any recommendation for testing women for hyperglycaemia during pregnancy must, therefore, be pragmatic, feasible, convenient and cost-effective. FBS in first trimester will help in establishing this.

Our aim is to find association between first trimester fasting blood sugar value compared with the second trimester oral glucose tolerance test value (75gm DIPSI criteria) for diagnosis of GDM. To find the efficiency of FBS and BMI as a screening test for GDM.

Early diagnosis and early intervention of diabetes is useful for improving pregnancy outcomes. FBS measurement at first prenatal visit or at the time of first booking will be useful to screen for previously undiagnosed pre-existing diabetes and also help to predict the development of GDM earlier.

## Materials and Methods

The study was conducted in the department of Obstetrics and Gynaecology, PSG Hospitals, Coimbatore from June 2014 – May 2015. The study period was 12 months.

**Study Design:** Prospective Observational Study

**Study Population:** 270 antenatal patients having antenatal follow up from 1<sup>st</sup> trimester in the department of Obstetrics & Gynaecology, PSG IMSR & Hospitals, Coimbatore.

**Inclusion Criteria:** All antenatal patients from first trimester of pregnancy, Singleton pregnancy

**Exclusion Criteria:** Pre gestational diabetes mellitus  
Patient who lost follow up for OGTT testing during 2<sup>nd</sup> trimester.

Patients with first trimester FBS more than 105mg/dl.

Antenatal patients on long term steroids for medical disorder.

## Methodology

The study was initiated after obtaining approval from the ethics committee in PSG IMSR.

The patients selected were according to the inclusion criteria- antenatal patients from first trimester without having pre-existing diabetes mellitus and oral and written consent were obtained.

Patients who had not turned up for OGTT during the second trimester or who were not willing to participate in the study were excluded.

Basic assessment of their risk factors was already done in the first antenatal visit along with detailed family history. Their height and weight was measured. Weight was noted at the time of first visit. BMI was calculated from the first visits data. Gestational age was noted for both the tests during first and second trimester.

About 270 antenatal mothers were selected during their first trimester from Obstetrics & Gynaecology department OPD during June 2014-May 2015 were explained about the study after excluding other women who were not eligible for the study and fasting blood glucose levels were measured and documented. The patients were followed up during the second trimester and a 75 grams OGTT was done and the levels were noted.

All the patients were asked to follow unrestricted carbohydrate diet and not to change the diet pattern and fasting blood glucose was tested during the first trimester with overnight fast of at least 8 hours.

During second trimester, when the patients entered the hospital for second trimester OGTT irrespective of the last meal given, 75gms oral glucose mixed in 150 ml of water and blood test taken 2 hrs later according to the DIPSI criteria. All the patients were instructed not to have meals after the 75gm glucose ingestion.

If the patient experienced nausea during the drinking procedure a pinch of fresh lime was added. If she had vomited after glucose ingestion then the testing is done at the further time of the day or asked to come on the following day for re-testing and the same procedure is followed. The patient is requested not to have meals in between and venous blood was collected 2 hrs later.

Two ml of venous blood was collected in sterile fluoride vial. These samples were centrifuged at 3500 rotation per minute for 10 minutes. Plasma was used for estimation. Blood test should be done within 3 hours of collection using autoanalyser, Cobas Integra 400 plus-Roche diagnostics by glucose hexokinase method using spectrometric assay. It has analytical sensitivity of 0.59mg/dl and test range of upto 720mg/dl.

## Test Principle:

Hexokinase catalyses the phosphorylation of glucose by ATP to form glucose 6 phosphate and ADP. To follow the reaction, a second enzyme glucose 6 phosphate dehydrogenase is used to catalyse oxidation of glucose 6 phosphate by NAD<sup>+</sup> to form NADH

D Glucose + ATP  $\xrightarrow{HK}$  Glucose 6 phosphate + ADP

D Glucose 6 phosphate + NAD + G6PD  $\rightarrow$  D-6-Phosphogluconate + NADH + H<sup>+</sup>

The concentration of NADH formed is directly proportional to glucose concentration. It is determined by increase in absorption at 340nm.

Patients with first trimester fasting blood glucose levels were categorised as <92 mg/dl, 92-105 mg/dl were included, >105 mg/dl were excluded from the study. Patients with FBS <92 mg/dl were subjected to second trimester 75 gms OGTT. Patients with FBS between 92-105 mg/dl were subjected to diabetic diet, FBS and PPBS was done after 2 weeks of diabetic diet and if it was found to be normal, they were subjected to second trimester 75 OGTT DIPSI criteria. If FBS, PPBS after 2 weeks of diabetic diet were high they were not subjected to second trimester OGTT and were excluded from the study. Patients with FBS of >105 mg/dl were excluded from the study.

First trimester FBS value and second trimester 75 gms GTT values were analysed and the results were tabulated. Correlation between first trimester FBS, BMI versus second trimester OGTT were done. Women diagnosed as GDM were managed appropriately.

Screening property of both fasting blood sugar and BMI were calculated and compared using receiver operating characteristic (ROC) curves.

## Results and Analysis

### Statistical Analysis:

1. First trimester FBS as a screening test for GDM
2. BMI as a screening test for GDM
3. BMI as a comparison for GDM
4. FBS as a comparison for GDM

**Table 1: First trimester fasting blood glucose as a screening test for gestational diabetes mellitus (statistical consolidated data)**

FBS Level		70	75	80	85	90	95	100
Patients > Threshold Value	Number of case	270	268	257	223	135	67	22
	%	100	99.2	95.1	83	50	24	8.14
Patients with GDM > Threshold Value	Number of case	15	15	15	15	13	5	1
False Positive Rate	%	100	99	91.7	81.6	47.9	24.4	8.3
Sensitivity	%	100	100	100	100	86.6	33.3	6.6
Specificity	%	0	0.78	8.3	18.9	52.1	75.6	91.7
PPV	%	5.5	5.6	5.8	6.7	9.6	7.5	4.5
NNP	%	100	100	100	100	98.5	95	94.4

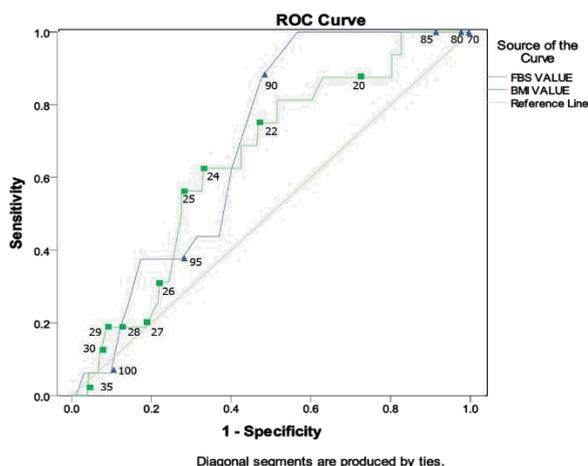
Patients with FBS>90 had sensitivity of 86.6%, specificity of 52.1%, Positive predictive value of 9.6%, negative predictive value of 98.5%.

**Table 2: I Trimester body mass index as a screening test for gestational diabetes mellitus (statistical consolidated data)**

BMI		20	22	24	25	26	27	28	29	30	35
Patients Threshold >	Numbers	199	129	92	78	58	40	30	25	20	3
	%	73.7	47.7	34	28.9	21.5	14.8	11.1	9.25	7.4	1.1
Patients with GDM > Threshold	Numbers	14	11	9	8	4	3	3	3	2	0
False Positive Rate	%	72.5	46.3	32.5	27.5	21.2	21.2	10.6	8.6	7.1	1.2
Sensitivity	%	93.3	73.3	60	53.3	26.7	20	20	20	13.3	0
Specificity	%	27.5	53.7	67.5	72.5	78.8	78.8	89.9	91.4	92.9	98.9
PPV	%	7	8.5	9.8	10.2	6.9	7.5	10	12	10	0
NNP	%	98.6	97	96.6	96	94.8	94.7	95	95.1	94.8	94.3

Patients with BMI >24 had sensitivity of 60%, specificity of 67.5%, positive predictive value of 9.8%, negative predictive value of 96.6%.

**Receiver operative characteristic curve**



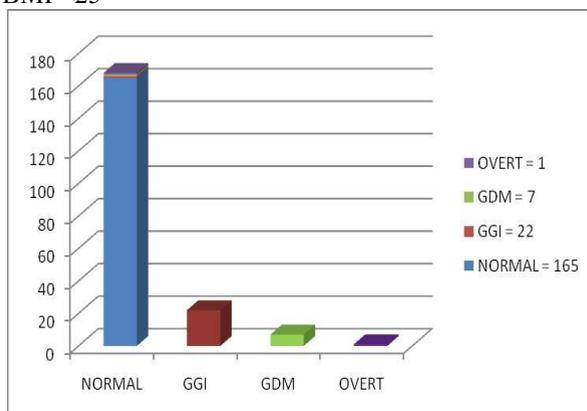
Area under curve for FBS=0.694  
 Area under curve for BMI=0.63

**Table 3: Body mass index as a comparison for gestational diabetes mellitus (cross tab)**

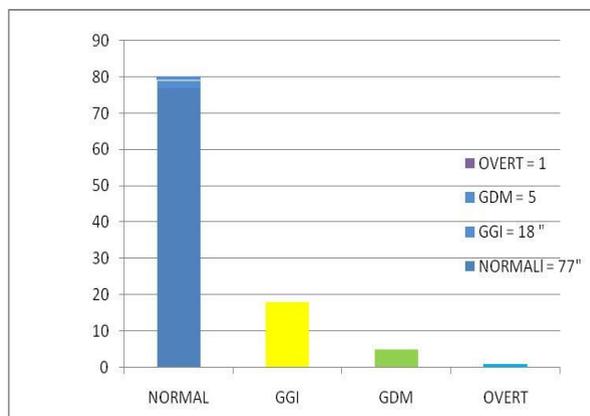
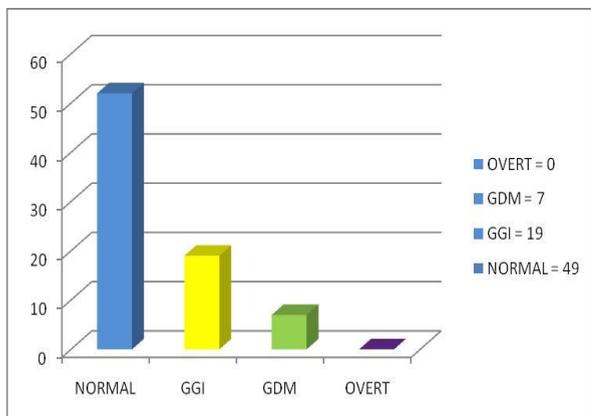
BMI VS GDM	OGTT			Total
	Normal	GGI	OVERT	
BMI <25	165	22	7	195
BMI >=25	49	19	7	75
Total	214	41	14	270

P value <0.01

**BMI <25**



**BMI >= 25**



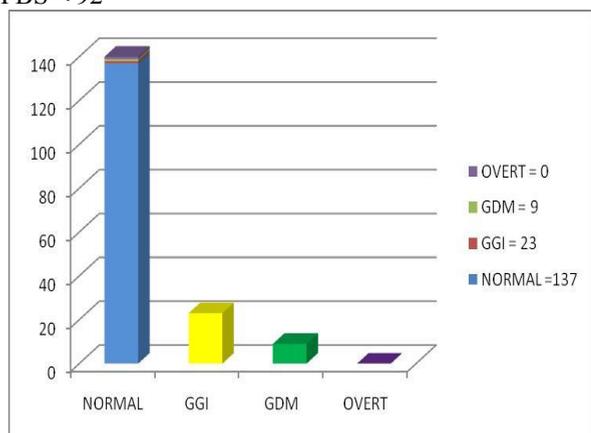
Out of 270 patients, patients who had BMI <25 had more normal values. Patients who had BMI ≥25 had increased GCT values. This data was found to be statistically significant.

**Table 4: Fasting blood sugar as a comparison for gestational diabetes mellites (cross tab)**

FBS VS GDM	OGTT				Total
	Normal	GGI	GDM	OVERT	
FBS <92	137	23	9	0	169
FBS ≥92	77	18	5	1	101
Total	214	41	14	1	270

P value =0.455

FBS < 92



FBS ≥92

In group I patients with FBS <92 were 169 patients, of which 23 developed GGI, 9 developed GDM. In group II FBS ≥92-105 were 101 patients out of which 18 patients developed GGI, 5 patients developed GDM, 1 patient developed overt diabetes respectively. Group II patients were subjected to diabetic diet earlier in view of initial high sugar values. So analysing the outcomes, we inferred that starting diabetic diet earlier has a significant role in decreasing the risk of developing GDM in advance pregnancy.

**Result**

Mean calculated continuous variable. Percentage calculated for categorical variable (sensitivity). Pearson chi –square test was used to find association between categorical variable.

In addition sensitivity, specificity, false positive, false negative were calculated. Receiver operating characteristic (ROC) curve was plotted to find cut off value for FBS & BMI for GDM.

Further Area under Curve (AUC) was calculated to observe discriminatory power between FBS & BMI. FBS(AUC=0.69) has little more discriminatory power in identifying GDM than BMI(AUC-0.63). P value <0.05 was considered statistically significant

All statistical analysis was done using SPSS Software (statistical package for social sciences) With a threshold of FBS>90, sensitivity of 86%, specificity of 52%, hence FBS >90mg/dl can be considered as a threshold value for predicting GDM which is lesser than the threshold 92 mg/dl which is already considered as a cut off for prediction of GDM. With a threshold of BMI>24, sensitivity of 60%, specificity of 67.5%, hence BMI >24 is a good predictor of GDM.

**Discussion**

Our aim was to find out the correlation between FBS and OGTT and to find the threshold value of FBS, BMI for developing GDM.

Out of 270 patients, 14 patients developed GDM which is 5.2% of the total study population. 1 patient developed overt diabetes which is 0.3% of study population.

Our study shows that pregnant women with FBS >90 mg/dl are more likely to develop GDM later in pregnancy and more likely to develop adverse pregnancy outcome if no intervention is done for these patients. Therefore, we suggest that women with Fasting blood glucose >90mg/dl who are more prone to develop GDM hence should be subjected to medical nutritional therapy. FBS (AUC=0.69) is a better than BMI (AUC=0.63) as a screening test for GDM.

Early diagnosis of gestational diabetes mellitus (GDM) is important to improve for both maternal and fetal outcomes. The burden of diabetes in India is very high. It is an urgent need to establish screening and diagnostic procedure which is easy, understandable and simple. FBS measurement is a well-tolerated and inexpensive routine examination.<sup>(2)</sup> FBS measurement has better test accuracy throughout the pregnancy.<sup>(3,4)</sup> Riskin-Mashiah et al.<sup>(2)</sup> study had high predictive value of first trimester FBS, and consider FBS as a screening test and not as diagnostic test with a suggested cut off value. This study concluded that, The FBS value lower than what is be considered as impaired fasting glucose, is associated with development of GDM. There is no clear cut off above which the risk of GDM is substantially increased. So for every 5 mg/dl increase in FBS or 3.5kg/m<sup>2</sup> increase in BMI there was 1.5 fold increased risk. First trimester fasting blood glucose value is an excellent test for determining the need to continue with the oral glucose tolerance test in the second trimester.<sup>(4,5)</sup>

The hyperglycaemia and adverse pregnancy outcome study estimated that Fasting blood glucose measurement identifies about 50% of all affected women without an additional 1 and 2 hour OGTT values.<sup>(6)</sup> Though previously FBS was neglected as a screening test for GDM, in high risk population it provides simple, practical algorithm to screen for GDM.<sup>(7)</sup> Riskin-Mashiah et al.,<sup>(8)</sup> has already reported that mild hyperglycemia in early pregnancy will lead to adverse pregnancy outcomes.

So instead of subjecting all patient to a glucose load to do OGTT in first trimester, which may aggravate nausea, vomiting which is more prevalent in first trimester. If patient vomits during the test, then OGTT has to be repeated again on another day which is time consuming. So, it is better to perform an easy, less time consuming, cost effective test that is fasting blood glucose.

Our study shows that pregnant women with FBS >90 mg/dl are more likely to develop GDM later in pregnancy and more likely to develop adverse pregnancy

outcome if no intervention is done for these patients. Therefore, we suggest that these women should be subjected to medical nutritional therapy. FBS as a screening test has little more discriminatory power in identifying GDM than BMI.

## Conclusion

Our study shows that FBS at first trimester will be helpful in the early prediction of gestational diabetes mellitus. Early diagnosis and early intervention of diabetes is useful for improving pregnancy outcomes. In conclusion, FBS measurement at first prenatal visit or at the time of first booking will be useful to screen for previously undiagnosed pre-existing diabetes and also help to predict the development of GDM earlier.

## References

1. Cousins L, Rigg L, Hollingsworth D, et al. "The 24-hour excursion and diurnal rhythm of glucose, insulin and C peptide in normal pregnancy" *Am J Obstet Gynecol* (1980);136:483.
2. Riskin-Mashiah S, Damti A, Auslender R "First trimester fasting hyperglycemia as a predictor for the development of gestational diabetes mellitus" *Eur J Obstet Gynecol Reprod Biol* (2010) 152:163–167.
3. Farrar D, Duley L, Lawlor DA "Different strategies for diagnosing gestational diabetes to improve maternal and infant health". *Cochrane Database Syst Rev*, (2011) Issue 10.
4. Agarwal MM, Dhatt GS, Punnose J "Gestational diabetes: utility of fasting plasma glucose as a screening test depends upon the diagnostic criteria" *Diabet Med* (2006);23:1319–1326.
5. Agarwal MM, Hughes PF, Punnose J, Ezimokhai M "Fasting plasma glucose as a screening test for gestational diabetes in a multi-ethnic, high-risk population". *Diabet Med* (2000);17:720–726.
6. Coustan DR, Lowe LP, Metzger BE, Dyer AR "The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study: paving the way for new diagnostic criteria for gestational diabetes mellitus" (2010). *Am J Obstet Gynecol* 202:654.e.16.
7. Maria I. Schmidt, Bruce B. Duncan, Angela J. Reichelt et al. Gestational Diabetes Mellitus Diagnosed With a 2-h 75-g Oral Glucose Tolerance Test and Adverse Pregnancy Outcomes. *Diabetes Care* July (2001) vol. 24no.7 1151-1155.
8. Riskin-Mashiah S, Younes G, Damti A, Auslender R. "First-trimester fasting hyperglycemia and adverse pregnancy outcomes. *Diabetes Care*". 2009;32(9):1639–1643.
9. Riskin-Mashiah S, Damti A, Auslender R "First trimester fasting hyperglycemia as a predictor for the development of gestational diabetes mellitus". *Eur J Obstet Gynecol Reprod Biol* (2010) 152:163–167.